IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.

: 10/625,989

Confirmation No.: 1706

Applicants

: Kenneth SETCHELL, et al.

Filed

: July 24, 2003

TC/A.U.

: 1616

Examiner

: Alton N. PRYOR

Docket No.

: 3515-104

Customer No.

: 6449

RULE 132 DECLARATION OF RICHARD L. JACKSON

I, Richard L. Jackson, declare as follows:

- 1. I am President and CEO of Ausio Pharmaceuticals, LLC, Licensee of the subject patent application.
- 2. My education and experience, which are further detailed in the copy of my resume that is attached hereto as Exhibit A, are as follows. I received a B.S. degree in chemistry in 1963 and a Ph.D. degree in microbiology in 1967, both from the University of Illinois. In addition to my current position as President and CEO of Ausio Pharmaceuticals, LLC, I have held Senior Executive positions in various pharmaceutical companies since the mid-1980's. I also have held numerous academic positions, including fellowships, associate professorships, and full professorships. Furthermore, I have established research centers at the University of Cincinnati College of Medicine and at Baylor College of Medicine, and I have received various honors and awards over the course of my professional career. I also have authored or co-authored hundreds of publications, I am a named inventor on 10 issued patents, and I have served or currently serve on approximately two dozen National Advisory Committees and Boards of Directors.

- 3. I am familiar with the subject patent application, including the currently pending claims. I am also familiar with the reference cited in the November 18, 2008 Final Office Action, by Alvira, et al.
- 4. I understand that the claims currently pending in this application recite various compositions relating to enantiomeric equol, particularly the R-enantiomer (R-equol).
- 5. In my capacity at Ausio Pharmaceuticals, I directed that a pharmacological screening study be undertaken to evaluate and directly compare the biological activities of R-equol, S-equol, and racemic equol in a collection of biochemical assays. Specifically, each of R-equol, S-equol, and racemic equol was screened against a broad spectrum of receptor systems using standard radioligand binding assay methods adapted from the scientific literature. The study was conducted by an outside party, with no interest in the present application, hired by Ausio specifically for the purpose of conducting the study. Attached hereto are descriptions of the study and the results obtained for each of S-Equol (AUS-131—Exhibit B), R-Equol (AUS-132—Exhibit C), and Racemic Equol (AUS-133—Exhibit D). As indicated, reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Percent inhibition results of the complete, broad spectrum of assays are reported.
- 6. I have reviewed the results of the study and, in my opinion, the results contain several examples of properties unexpectedly possessed by the enantiomeric forms of equal that are not possessed by the racemic mixture. Moreover, the overall results reveal that a commonly held position, namely that only one of the two enantiomers in a known active racemic

mixture is presumed active, is not universally applicable with respect to equol. As the data reveal, in some systems, the S-enantiomer is active while the R- is not. In others, the R-enantiomer is active while the S- is not. In some systems, both enantiomers and the racemate are active, and in one particular system, discussed more fully below, both the S- and R-enantiomers are similarly active, but the racemate is <u>inactive</u>. It is also seen that there is variability in activity between related receptor types.

7. The table below summarizes some of the more significant individual results obtained in the broad spectrum of studies, as referred to above.

In vitro Pharmacological Screening

Target	Percent I	nhibition (a	t 10 uM)	Interpretation (re:
	S-Equol	R-Equol	Racemate	higher values)
ERα	92	93	94	Positive control
ERβ	98	94	98	Positive control
src Protein Tyrosine Kinase LCK	27	26	1	Oncology indication
Transcription Response Factor, NF-AT	5	32	19	Anti-inflammatory indication, potential MOA
G Protein-coupled Receptor 103	58	14	38	Bone sparing, satiety, CNS effects, inflammation
Monoamine Transporter	16	51	49	CNS, antidepressant
NE Transporter	57	37	50	Antidepressant
Dopamine Transporter	84	88	92	Anti-Parkinsonism

As is clear from the table, the approach of simply resolving a racemate into its separate enantiomers, determining which of the two isomers is the active form (and which is the inactive form), and consequently choosing to prepare a composition using the active form, would not appear to be effective with respect to equal. In my opinion, one could not reliably predict biological activity of the equal enantiomers when armed only with teachings concerning the racemic mixture.

- 8. The src Protein Tyrosine Kinase (LCK) data provides a clearly surprising and unexpected result. LCK is an important receptor kinase that regulates the growth of cells. When mutated, uncontrolled growth occurs. The studies here have shown that both S- and R-equol inhibit this activity approximately equally (27% and 26% respectively at 10 µM concentration). However, racemic equol, which of course contains both R- and S-equol, surprisingly does not inhibit the activity (1% inhibition at the same 10 µM concentration). This is a completely unexpected finding. Based on these results, therefore, racemic equol would likely be ineffective in inhibiting cancer growth, for example, but a composition containing the R-enantiomer, as claimed herein, would surprisingly be expected to show potential benefits.
- 9. The results obtained in the study referred to herein are surprising and would not be expected to be achieved based on the teachings in the reference noted in the November 18, 2008 Final Office Action (Alvira, et al.), or the teachings in the other references of record. Specifically, one could not assume enantiomeric equal compositions would be biologically active or otherwise useful based merely on teachings concerning racemic equal.

U.S. Application No. 10/625,989 Rule 132 Declaration of Richard L. Jackson

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed:

Richard L. Jackson, Ph.D.

President and CEO

Ausio Pharmaceuticals, LLC

Date:

6/30/09

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RICHARD L. JACKSON, PhD

CURRENTPOSITION

Austo Pharmaceuticals, LLC President and CEO 1776 Mentor Ave. Cincinnati, OH 45212 613.731.0333

Richard@auslopharma.com

A specialty pharmaceutical start-up company focused on the development of various medicines. The Company's first drug product is AUS-131 which was ilcensed from Cincinnati Children's Hospital and Sanitarium, an Australian health food company. The compound currently is being developed as an oral drug. A topical formulation also is being developed. The first clinical studies will begin in Q1, 2008.

PREVIOUS POSITIONS

ENTREPRENEUR-IN-RESIDENCE, Cincinnati Children's Hospital

2003 - 2006

Provided pharmaceutical and commercial input into the Computational Medicine Center proposal; a \$28 million grant was awarded to Cincinnati Children's Hospital from the State of Ohio (Third Frontier Award).

Provided Input for the Tomorrow Fund, a Third Frontier award to establish a seed fund at Children's Hospital.

Provided pharmaceutical and drug development expertise for the development of technologies from Children's Hospital. Several technologies were licensed to pharmaceutical companies. Ausio Pharmaceuticals, LLC, Bexlon Pharmaceuticals, LLC and Atabios Therapeutics are companies that have been spun-out from these efforts.

EMERGEN, INC., Salt Lake City, UT

March 2002 - April 2003

President and CEO Chairman, Board of Directors

in-licensed leuprogei from Atris Laboratories for the treatment of endometriosis. The research focus was the genetic basis of endometriosis and polycystic ovary syndrome. Identified novel targets for invasive cancers by understanding placental blology.

ATRIX LABORATORIES, INC., Fort Collins, CO

November 1, 1998 - 2002

Senior Vice President, Research and Development Reported to Mr. D.R. Bethune (CEO & Chairman) Member of Board of Directors

Responsible for preclinical, clinical, regulatory, and quality activities for new therapies in dermatology, pain management, and oncology. Five products reached the market place,

WYETH-AYERST, the Pharma Division of American Home Products

1993 - 1998

Senior Vice President, Discovery Research Reported to Dr. R.I. Levy (President, Wyeth-Ayerst Research) Deceased

Responsible for the discovery of innovative, new therapies for Women's Health, Neurological Disorders, Cardiovascular and Metabolic Diseases, Infectious Diseases, Oncology and ImmunoInflarmmatory Diseases. Provided strategic, scientific and administrative leadership for

the worldwide research efforts. Responsible for 1100 people with an annual internal operating budget of \$180 million plus external University and Biotech alliances of \$52 million. Seven products reached the market place.

MARION MERRELL DOW RESEARCH INSTITUTE

1985 - 1992

Senior Vice President Discovery Research

Reported to Dr. A. Sjoerdsma/Dr. W. Lovenberg (Presidents - MMD Research Institute)

Responsible for the discovery of drugs for Allergy, Pulmonary Diseases, CNS Disorders, Oncology, Cardiovascular/Metabolic Diseases and Immuno-Inflammatory Diseases. Responsibility for the US discovery operation (350 scientists) with close working relationships with Center Directors in Strasbourg, France, and Milano, Italy.

UNIVERSITY OF CINCINNATI COLLEGE OF MEDICINE

1978 - 1984

Head, Division of Lipoprotein Research Professor, Department of Pharmacology and Cell Biophysics, Biological Chemistry and Medicine

Department Chairman: Dr. A. Schwartz

Established a research center of excellence in cardiovascular diseases.

BAYLOR COLLEGE OF MEDICINE

1971 - 1977

Associate Professor, Departments of Medicine and Cell Biology Department Chairman: Dr. A.M. Gotto, Dr. B. O'Malley

Established a cardiovascular center for research, patient care and education.

NIH, LABORATORY CHEMICAL PATHOLOGY, NIAMD

1970 - 1971

Senior Staff Fellow

NIH, EXPERIMENTAL THERAPEUTICS, NHLBI

1969 - 1970

Junior Staff Fellow

BROOKHAVEN NATIONAL LABORATORY

1967 - 196B

Postdoctoral Fellowship

PROFESSORSHIPS

HADASSAH UNIVERSITY HOSPITAL, Jerusalem, Israel (November - December, 1974)

STATE UNIVERSITY OF UTRECHT, Utrecht, the Netherlands (January - July, 1978)

Biochemical Laboratory

INSTITUTO VENEZOLANO DE INVESTIGACIONES CIENTIFICAS, Caracas, Venezuela

(October, 1982)

NATIONAL CARDIOVASCULAR CENTER RESEARCH INSTITUTE, Osaka, Japan (June -August, 1984)

ROCKEFELLER UNIVERSITY, New York (January - July, 1985)

EDUCATION

HONORS	
AWARDS	1969 American Cancer Society Postdoctoral Fellowship
	1972 American Heart Association Established Investigator
	1974 American Heart Association Lewis Katz Award
	1981 The 1000 Contemporary Scientist Most Cited 1985 – 1978
	1984 Naito Foundation Award - National Cardiovascular Research Institute,
	Osaka, Japan
NATIONAL	1979 – 1983 NiH Metabolism Study Section
ADVISORY	
COMMITTEES/	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
BOARD OF	Antiger Comment of the Comment
DIRECTORS	
DIVER! AV	1982 – 1988 Editorial Board, Journal of Lipid Research
	1988 – 1992 Associate Editor, Journal of Lipid Research
	1990 - 1992 American Heart Association, Executive Committee at Large
	1991 - 1992 University of Cincinnati Cardiovascular Center, Advisory Board
	1992 – 1997 Editorial Board, Current Drugs in Research
	1992 – 1995 Arthritis Foundation, Scientific Advisory Board
	1994 – 1998 American Heart Association, Long-Term Planning Committee
	1995 – 1998 Rider University, Scientific Advisory Board
	1996 – 1998 Immunex Corporation, Member Board of Directors
	1997 – 2000 Princeton University, Chemistry Department Advisory Board
	1998 – 2000 ZymoGenetics, Scientific Advisory Board
	1999 – 2002 Atrix Leboratories, Member Board of Directors
	2001 - 2007 Inflazyme, Member Board of Directors
	2002 - 2003 EmerGen, Inc., Member Board of Directors
	2003 - Present Oncothyreon (Biomira), Member Board of Directors
	2003 - 2005 MDS Capital, Scientific Advisory Board
	2005 AB Biopharma, Member Board of Directors
	2006 - Present Bexion Pharmaceuticals, Chairman, Board of Directors
	2008 - Present Viron Therapeutics, Chairman, Board of Directors
	2007 - Present Leukemia and Lymphoma Society, Member Board for Translational Research
	2007 - Fresent Cenkenna and Cymphonia Society, Wember Board for Translational Research
PUBLICATIONS	274 Reviewed Articles
	Over 500 Abstracts and Presentations
	·
PATENTS	10 Issued Patents

SpectrumScreen Data Report Ausio Pharmaceuticals LLC

Study Completed: August 27, 2007
Report Printed: August 27, 2007

MDSPS PT#: 1094967

Alt. Code 1: Batch: A313-10-5

Alt. Code 2:

Alt. Code 3:

Sample(s): AUS-131

M.W.: 242.27

Objectives:

To evaluate, in SpectrumScreen, the activity of test compound AUS-131 (PT# 1094967).



PTW: CODE: 1094967 AUS-131

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MDS Pharma Services Pharmacology Data Report On Compound AUS-131 For Ausio Pharmaceuticals LLC

Work Order Number:

1-1028408-1

Services Being Reported: SpectrumScreen

Alternative Work Order No:

Purchase Order Number:

Total # of Assays: 159

Compound Information:

Compound Code:

AUS-131

Alternative Code 1: Batch: A319-10-5

Alternative Code 2: Alternative Code 3:

MDSPS Internal #:

1094987

Notecular Weight:

242.27

Sponsor:

Ausio Pharmaceuticals LLC 1776 Memor Avenue

Suite 340

Cinchnali, OH 45212 USA

Undertaken et:

MDS Pharma Services - Taiwan Ltd.

Pharmacology Laboratories 158 U-Teh Road, Peltou

Talpel, Talwan 112 Talwan

Date of Study:

August 13, 2007 - August 27, 2007

Study Directors:

Kun-Yuan Lin, MDS Pharma Services - Talwan Lid. Kuo-Hsin Chen, MDS Pharma Services - Talwan Ltd.

Distribution:

Auslo Pharmaceuticals LLC

"This study was conducted according to the procedures described in this report. All data presented are sutherfac, accorded and correct to the best of our knowledge."

Kun-Yuan Un

Study Director for Animal Assays

Kem- Juan Lin

Kno-Hain Chen

Koo- Nia C

Study Otrector for Blochemical Assays

\$ Sin

Jam-Wu Wel, Ph.D

Quality Control and Data Reviewer

Jiam - Wei Wei

Peter Chiu, Ph.D

Technical Director

PT 8: 1094961

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SUMMARY

STUDY OBJECTIVE

To evaluate, in Radioligand Binding assays, the activity of compound AUS-131 (PT# 1094967).

METHODS

Methods employed in this study have been adapted from the scientific literature to maximize reliability and reproducibility. Reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Assays were performed under conditions described in the accompanying "Methods" section of this report. The literature reference(s) for each assay are in the "Literature References" section. If either of these sections were not originally requested with the accompanying report, please contact us at the number below for a printout of either of these report sections.

Where presented, IC_{50} values were determined by a non-linear, least squares regression analysis using Data Analysis ToolboxTM (MDL Information Systems, San Leandro, CA, USA). Where inhibition constants (K) are presented, the K₁ values were calculated using the equation of Cheng and Prusoff (Cheng, Y., Prusoff, W.H., Biochem. Pharmacol. 22:3099-3108, 1973) using the observed IC_{50} of the tested compound, the concentration of radiologand employed in the assay, and the historical values for the K₀ of the ligand (obtained experimentally at MDS Pharma Savicas). Where presented, the Hill coefficient (h₀), defining the slope of the competitive binding curve, was calculated using Data Analysis ToolboxTM. Hill coefficients significantly different than 1.0, may suggest that the binding displacement does not follow the laws of mass action with a single binding site. Where IC_{50} , K₀, and/or r₀, data are insufficient to be quantitative, and the values presented (K₀, IC_{50} , r₀) should be interpreted with caution.

PESULTS

A summary of results meeting the significance criteria is presented in the following sections. Complete results are presented under the section labeled "Experimental Results". Individual responses, if requested, are presented in the appendix to this report.

SUMMARY/CONCLUSION

Significant results are displayed in the following table(s) in rank order of potency for estimated IC, and/or K, values.

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SUMMARY OF SIGNIFICANT PRIMARY RESULTS

Biochemical assay results are presented as the percent inhibition of specific binding or activity throughout the report. All other results are expressed in terms of that assay's quantitation method (see Methods section).

- For primary assays, only the lowest concentration with a significant response judged by the assays' criteria, is shown in
- Where applicable, either the secondary assay results with the lowest dose/concentration meeting the significance criteria
 or, if inactive, the highest dose/concentration that did not meet the significance criteria is shown.
- Unless otherwise requested, primary screening in duplicate with quantitative data (e.g., IC50± SEM, KI± SEM and nH) are shown where applicable for individual requested assays. In screening packages, primary screening in duplicate with semi-quartitative data (e.g., estimated ICSO, KI and nH) are shown where applicable (concentration range of 4 log units); available secondary functional assays are carried out (SO µM) and MEC or MIC determined only if active in primary assays >50% at 1 log unit below initial test concentration.
- Please see Experimental Results section for details of all responses.

Significant responses (2.50% inhibition or attinutation for Biochemical assays) were noted in the primary assays listed below:

		PRIM	ary tests			
CAT.#	PRIMARY BIOCHEMICAL ASSAY	SPECIES	CONC. % INH.	iC**	K,	r _e
204410	Transporter, Norepinephrine (NET)	hum	10 µM 57		· · · · · · · · · · · · · · · · · · ·	********
220320	Transporter, Dopamine (DAT)	hum	10 µM 84			
25010	Estrogen ERa	hum	10 µM 92			
26050	Estrogen ERB	hum	58 Mu 01			
226300	G Protein-Coupled Receptor GPR103	hum	10 µM 68			

Pertially educte in in vitro test solvent.
 A standard error of the mean is presented where results are based on multiple, independent determinations. go-guines pig; hem-hamster; hum-human

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat.#	TARGET	BATCH	SPP.	D=	CONC.		†% INE	UBI	HOE	IC ₅₀	. қ		M	
							-108 -30	0 9	100			'	'n	
						%	1 1	1 1	1					_
200510	Adenosine A ₃	203049	hum	2	10 µM	√8		d						
200810	Adenosine A ₂₄	203063	trum	2	10 pM	22								
200720	Adenosine As	203104	hum	2	10 gtM	9								
203100	Adrenergic or _{th}	203043	ret	2	10 µM	o								
203200	Adrenergic au	203044	rat	2	10 µM	6		h						
203400	Adrenergic cro	203045	hum	2	10 µM	14		E						
203820	Adrenergic a _{IA}	203046	hum	2	10 pM	-3								
203800	Adrenergic ox	203048	hum	2	10 µM	-2								
204010	Adrenargic \$1	203050	hum	2	10 µM	-2	!	ı						
204110	Adrenergic β ₁	203051	hom	2	10 µM	8		lı						
204200	Adrenergic β ₃	203052	hum	2	10 pM	-3		1						
204480	Adrenomedullin AM ₁	203480	hum	2	10 µM			1						
204470	Adrenomedullin AM ₂	203481	hum	2	10 µM	9		1						
204600	Aldosterone	203107	rat	2	10 µM	9		1						
205000	Anaphylatoxin CSa	203237	hum	2	10 pM	1		h						
285010	Androgen (Testosterone) AR	203102	rat	2	10 µM	5		1						
210020	Angiotensin AT ₁	203406	hum	2	10 µM	8		1						
210110	Angiotensin AT ₂	203035	hum	2	10 µM	3		l						
210700	AP)	203462	hum	2	10 µM	12								
211000	Atrial Natriuretic Factor (ANF)	203189	2	2	10 µM	ન્ડ		ıl						
211600	Bombesin 881	203463	hum	2	10 pb4	9	•	1						
211700	Bombesin BB2	203464	hum	2	10 µM	1		b						
211800	Bornbesin BB3	203485	hum	2	10 µM	-7		ď						
212510	Bradykinin B,	203088	hum	2	10 µM	8		1						
212610	Bradyldnin B _a	203087	hum	2	10 µM	8		1						
213810	Calcitonin	203238	hum	2	10 µM	1		þ						
	Calcitorin Gene-Related Peptide CGRP ₁	203239	hum	2	10 µM	-19	1							
	Calcium Channel L-Type, Benzothiazepine	203056	rat	2	10 pM	-8	1							
	Calcium Channel L-Type, Dihydropyridine	203057	rat	2	10 pM	5		þ						
	Calcium Channel L-Type, Thenylzikylamine	203058	ret	2	10 µМ	34		22						

gp-guines pig; hars-hamster; hum-human

^{*} Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble is in vitro test solvent.

• Denotes liam meeting criteria for significance

† Results with ≥ 50% stimutation or inhibition are highlighted. (Negative values correspond to <u>stimutation</u> of binding or enzyme activity)

R—Additional Comments

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cet. #	TARGET	BATCH*	SPP.	10=	CONC.		†% INI	HIB	Ш	ON	IC ₅₀	K		Π _M	I
		•				96	·100 ·50 ↓ ↓	÷	\$	100				· / II	·
216000	Calcium Channel N-Type	203178					<u> </u>	Ť	*	*		 <u> </u>			
217020	Cannabinoid CB ₁		rat	2	10 µM	O		L							
217100	Carnabinoid CB ₃	203177	hum	2	10 µM	" 8		ŀ		l					
244600		203178	hum	2	10 µM	-6		1							
218010	Chemokine OCICR1	203471	hum	2	10 µM	5		E							
218120	Chalecystokinth CCK, (CCK)	203409	hum	2	10 المنز	13		F							
219100	Chalegystakinin CCK, (CCK)	203488	מועה	2	المرا 10	8		1							
	Colchicine	203000	rat	2	10 jak	15									
219150	Corticotropin Releasing Factor CRF ₁	203409	hum	2	الشر 10	-2		4							
219500	Dopamine D ₁	202962	hum	2	10 µM	6		h		ı					
219700	Dopamine D ₂₅	202964	hum	2	10 pM	-1		ſ		- 1					
219800	Dopamine D ₃	202965	hum	2	10 pM	3		1							
219900	Dopareine Day	202986	hum	2	10 pt4	19			ł						
220200	Dopamine D _s	202969	hum	2	10 µM	5		F		1					
224010	Endothelin ET _A	203091	hum	2	10 µM	-6		ď		1					
224110	Endothelin EY,	203092	hum	2	10 JM	12		h		- 1					
225510	Epidermal Growth Factor (EGF)	203167	hum	2	10 µM	9		F							
225800	Erythropoletin EPCR	203467	hum	2	10 µM	6		ĥ							
226010	Estrogen ERa	202976	מושל	2	10 µM	92		H							
228060	Estrogen ERB	202977	hum	2	10 µM	98			÷				•		
228300	G. Protein-Coupled Receptor GPR1 03	202993	hum	2	10 µM	58									
226230	G Protein-Coupled Receptor GPR8	203470	hum	2	Mu 0f	4		1							
225810	GABA _{in} Chloride Channel, TBOB	203101	rat	2	10 µM	0				İ					
226600	GABA, Fluistrapeparii, Central	203061	rat	2	10 μΜ	12									
226500	GABA _A Muscimol Central	203060	rat	2	10 μ3Α	-4		ıl		ı					
228610	GABA	203158	hum	2	10 µM	-20		1		ı					
228710	GABA _{SIB}	203159	hum	2	10 yald	-8	, [-					
230000	Gebapentin	203001	rat	2	10 µM	0		1		- 1					
231510	Galanin GAL1	203165	מעול	2	10 µ3A	-1		1		- 1					
231600	Gatanin GAL2	203168	hum	2	10 µM	4		i		- 1					
232600	Glutamete, AMPA	203157	rat	2	10 pM	-19		1		Ì					

^{*} Batch: Represents compounds tested concurrently in the same assay(s), \$ Particly soluble in in vitro test solvent.

gp-guinea pig; ham-hamster, hum-human

Denotes item meeting criteria for eignificance
 Results with 2 50% etimulation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)
RaAdditional Comments.

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Cat.#	Target	BATCH	SPP.	- 13 50	CONC.		†% INI	UBITION	IC _{so}	K _i	n _H	R
						95	-100 -50 1 1	, z 100		-1	* 48	
232700	Glutamate, Kainate	203063	ræl	2	10 µM	10	\ <u>*</u> *	1				
232810	Glutamate, NMDA, Agonism	203064	rat	2	10 µM			ļ				
232910	Glatzmate, NIMDA, Glycine	203065	rat	2	10 µM	-1	•	1				
233000	Glutamate, NMDA, Phencyclidine	203068	rat	5	10 µM	-8	:					
234000	Gutamate, NMDA, Polyamine	203087	rat	2 .	10 иМ	-5		2				
238000	Glydne, Strychnine-Sensitive	203068	ret	2	Mu OI	3		1,				
239300	Growth Hormona Secretagogue (GHS, Ghrelin)	203243	hum	2	المر 10	6		ľ				
289610	Histamine H ₁	202970	hum	2	10 uM	8						
239710	Histamine H ₃	203069	hum	2	10 uM	8		,				
239810	Histamine H	202972	hum	2	10 µM	-9		•				
238900	Histamine H,	202978	hum	2	10 µM	4	ľ					
241000	Imidazoline i _e , Central	202974	rat	2	10 µM	-6	1					
242500	Inositol Trisphosphate IP3	203244	rat	2	70 µM	16						
243000	Insulin	203206	rat	2	10 µM	-9						
250400	Leptin	203317	mouse	2	10 µM	.9						
250510	Leukotriene, SLT QTBL)	204039	ham	2	10 pM	9		1				
250460	Leukotriene, Cysteinyl CysLT,	203089	hum	2	10 µM	-1						
250480	Leukatriene, Cystelnyl Cysl.T ₂	203090	hum	2	المر 10	-21		1	is			
251100	Melanocortin MC	203411	hum	2	10 µM	6	_	' l,				
251300	Melanocortin MC ₂	203412	hum	2	10 µM	-3		. [
251850	Melanocortin MC _d	203413	hers	2	10 µM	1		'				
251400	Melanocortin MCs	203414	hum	2	10 µM	18		3				
251600	Melatonin MT,	203140	hum	2	10 µM	5		,				
251700	Melistonin MT ₂	203142	hum	2	10 µM	41						
252200	Motilin	203472	hum	2	10 pM	8						
252810	Muscarinic Ma	202857	hum	2	10 µM	-9	1					
252710	Muscarinic Ma	202958	hum	2	10 pM	a	,	1 1				
252810	Muscariale M	202959	hum	2	10 pMs	1		h I				
252910	Muscarinic Ma	202980	hum	2	10 µM			ľ I				
258010	Muscarinic Ms	202981	hum	2	10 µM	-1	į	ļ [
	N-Formyl Papilde Receptor FPR1	203240	hum	2	10 jdM	-5	i					

^{*} Betch: Represents compounds tested concurrently in the same assay(s). \$ Partially soluble in in vitro test solvent.

⁻ Denotes item meeting criteria tessed concurrency in the same assay(s). ‡ Partially soluble in in vitro test ectivent.

- Penotes item meeting criteria for significance

- Penotes item neeting criteria from or inhibition are highlighted. (Negative values correspond to <u>stignification</u> of binding or enzyme activity)

- Re-Additional Comments

- GP-guines pig; hern-harmster; hum-human

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cot. #	TARGET	BATCH	SPP.		CONC.		†%	INE	IIB.	TTO	N	iC _{so}	K	n _n	1
•		٠.			•					50 i	100		• •	. •••	
	i					95	1	1	†	1.	ᅬ		•		
226200	N-Farmyl Peptide Receptor- Like FPRL1	203241	bum	2	10 µM	-10		i							
258100	Neuromedin U MMU,	203473	hum	2	10 µM	2			h						
258200	Neuromedin U HMU:	203474	hum	2	10 µM	5			•		1				
257010	Neuropeptide Y Y ₁	203099	hum	2	10 µM	-10		ı	ıľ		-				
257110	Neuropeptide Y Y ₂	203094	វាបាពា	2	10 μάν	4		Ī	h						
258010	Neurotensin NT ₁	203318	hum	2	10 pM	7			ſ		ļ				
258590	Nicotinic Acetylcholine	202989	hun	2	10 µM	-1	1		d						
258700	Nicotinic Acetylcholine o'l, Bungarotoxin	802991	hum	2	10 μм	10									
258830	Nicotinic Acatylchaline a7, Bungarotosin	202990	rat	2	10 µM	-6		j							
260110	Oplate 5 (OP1, DOP)	203070	hum	2	10 µM	8			l		ı				
280210	Oplate x (OP2, KOP)	203072	hum	2	10 pM	12					ı	•			
260410	Oplate µ (OP3, MOP)	203074	hum	2	10 µM	-6	ļ	ı							
260600	Orphanin ORL;	203478	hum	2	10 µM	2			1						
264500	Phorbol Ester	203078	mouse	2	10 JMJ	1	l		h		ı				
265010	Platelet Activating Factor (PAF)	203007	hum	2	10 pAJ	6			ı		١				
265200	Platelet-Derived Growth Factor (PDGF)	202979	mouse	2	10 pM	9									
265500	Potassium Channel DG	203079	rat	2	10 JAN	3			h		ı				
265600	Potassium Channel [Kgr]	203078	ham	2	10 pol	8					- 1				
265800	Potassium Channel (SKo.)	203002	ret	2	10 µM	4			Ī		١				
285900	Potassium Channel HERG	202994	hum	2	10 µM	9	l								
268020	Progesterone PR-8	202992	hum	2	10 µM	15									
288030	Prestanoid CRTH2	203352	hum	2	10 104	. 16					١				
188050	Prostanoid DP	202995	hum	2	10 µM	30				1	-				
288200	Prestanoid EP ₂	202998	hum	2	10 µM	17	ļ				ŀ				
68410	Prestanoid EP4	202897	hum	2	10 pM	5			li						
85 510	Prostanoid, Thrombourne A ₂ (TP)	203004	hun	2	10 pM	4			Ī						
68700	Purinergic P ₂₈	202982	rebbit	2	10 µM	-12		Ŀ			١				
168810	Purinargic Par	202983	rat	2	10 pM	5		Ī	1		-	-			
88500	Retinoid X Receptor RXRa	203477	hum	2	10 µM	٥			ľ		- (

gp-guines plg; ham-hamster; ham-human

^{*} Satch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in *In vitro* test solvent.

• Denotes item meeting criteria for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)

= A-A-referent Comments R-Additional Comments

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Cat	TARGET	BATCH	SPP		CONC.		1% INH	IBITI	ON	IC _{so}	K	n	F
	<u>:</u>	•		•	•	95		1 1	180	.020	, . 	****	•
270000	Rollpram	203130	rat	2	10 pM	8		,			•		_
270300	Ryanodine RyR3	203478	rat	2	10 µM	7			- 1				
271 110	Serotonin (S- Hydroxytryptam(ne) S-HTsa	203108	jmu	2	10 µM	-5	ı						
271200	Serotorin (5- Hydroxybyptamine) S-HT ₁₈	203109	nat	2	10 µM	22			·				
271700	Serotonin (5- Hydroxytryptamine) S-HT ₂₈	203251	hura	2.	10 JAM	17		9					
271800	Serotonin (5- Hydroxytryptamine) 5-HT _K	203273	hum	2	10 pA	15		2					
271910	Serotonin (3- Hydroxytryptamine) S-HT,	203164	hum	2	10 µM	-11	•						
272000	Serotonia (S- Hydrogtryptamine) S-HT ₄	203174	₽	2	10 µM	4		1					
272100	Servionin (S- Hydrwytrypiamina) S-HT ₂₄	203003	hum	2	10 µM	9		ı					
272200	Serotonin (5- Hydroxytryptomine) 5-HT ₆	203254	hum	5	10 µM	11		3					
278110	Sigma o ₁	203082	hum	2	10 µM	18		2					
278200	Sigma o _i	203083	rat	2	10 pM	15							
279510	Sodium Channel, Site 2	203084	rat	2	10 µM	2		1		!			
282510	Somatustatin esti	203181	hum	2	10 µM	14							
282700	Somatostatin sst2	203182	hum	2	10 pds	3		5					
282530	Somatostatin sst3	203183	hom	2	10 µM	-1	1	ľ					
282900	Somatostatin sst4	203184	hum	2	10 µM	8	ľ	h					
283000	Somatostalin sst5	203188	hum	2	10 μM	-5	ı	[
266510	Tachykinin NK,	203160	hum	2	10 µM	-2	'i	!					
255800	Tachykinin NK	203181	hum	2	10 µM	25		-					
255710	Tachyldain NK,	203162	hum	2	10 µM	-5							
286900	Thyroid Hormone	203171	rat	2	10 µM	-7	1						
286000	Thyrotropin Releasing Hormone (TRO)	203259	ret	2	10 µM	8	•	1					
200288	Transforming Growth Factor-β (TGF-β)	202980	mouse	3	10 µМ	11		•					
202000	Transporter, Adenosine	203088	gp	2	10 pM	6							
19000	Transporter, Choline	203105	mat	2	10 µM	10		1	ı				

Betch: Represents compounds tested concurrently in the same assay(a). ‡ Partially soluble in In vitro test solvent.
 Denotes item meeting criteria for eignificance
 † Results with ≥ 50% ethnutation or inhibition are highlighted. (Negative values correspond to <u>stimutation</u> of binding or enzyme activity)
 Re-Additional Comments
 gp-guines pig: hem-hamster; hum-human

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Cat.#	TARGET	ватсн•	SPP.	15= 	CONC.	% J	MO S S S S S S S S S S S S S S S S S S S	IC _{so}	K.	n _{el}	R
₹ 220320	Transporter, Doparnine (DAT)	203188	hum	2	10 µM	. 84		÷			
228400	Transporter, GABA	203059	rat	2	10 µM	8	1		٠		
252010	Transporter, Monoamine	208179	fidden	2	10 µM	16					
2044 10	Trafsporter, Norepinephrine (NET)	203581	hum	2	10 ⁻ µM	57			•		
274030	Transporter, Serotonin (S- Hydroxytryptamine) (SERT)	203055	hum	2	10 µM	11)	!		•	
288700	Urotensin II	203234	hum	2	10 µM	-14					
286810	Vanilloid	203133	rat	2	10 µM	-6	i				
288900	Viscular Endothelial Growth Factor (VEGF)	203598	hum	2	10 µM	26					
287010	Vasoactive Intestinal Peptide VIP ₁	203269	hum	2	10 µM	0	1				
287520	Vesopressin V _{IA}	203097	hum	2	10 µM	2	h				
287580	Vesopressin V _{II}	203098	hom	2	10 μ04	-1					
287810	Visopressin V ₂	203099	hurp	2	10 µM	-20					
288000	Vitamin D ₃	203096	hum	2	10 µM	-8	71	•			

^{*} Beach: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in in vitro test solvent.

• Denotes have meeting orienta for eignificance
† Results with ≥ 50% comutation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)
R=Additional Comments
gp=guinea pig; ham-hamster; hum-human

FIV: 1094967 CODE: ADS-121

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

MDS has an exclusive, worldwide limited use license trom Synaptic Pharmaceutical Corporation to perform these assays: Advenergia Alpha 1D, Advenergia Alpha 2B, and Departine D5 for aniety and selectivity profiling. MDS license excludes performing those assays in connection with drug discovery or development activities where the principal therapeutic mechanism of action of the test compound involves selective binding to a licensed receptor. Customers may contact Synaptic directly it they believe they need a broader license.

SpectrumScreen Data Report Ausio Pharmaceuticals LLC

Study Completed: August 27, 2007 Report Printed: August 27, 2007

MDSPS PT#: 1094968

Alt. Code 1: Batch: A313-84-1

Alt. Code 2:

Alt. Code 3:

Sample(s): AUS-132

M.W.: 242.27

Objectives:

To evaluate, in SpectrumScreen, the activity of test compound AUS-132 (PT# 1094968).



PTW: CODE:

109-0068 AUS-132

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MDS Pharma Services Pharmacology Data Report On Compound AUS-132 For Ausio Pharmaceuticals LLC

Work Order Number:

1-1028408-1

Services Being Reported: SpectrumScreen

Alternative Work Order No:

Purchase Order Number:

Total # of Assays: 159

Compound briarmations

Compound Code:

AU8-132

Alternative Code 1:

Batch: A313-84-1

Alternative Code 2:

Alternative Code 3:

1094858

MDSP8 Internal #: Moincular Weight:

242.27

Sponsor:

Austo Pharmaceuticets LLC

1776 Mentor Avenue Suite 340

Cinchnati, OH 45212

Undertaken et:

MDS Pharma Services - Tahran Ltd.

Pharmacology Laboratories 158 Li-Teh Fload, Petrou

Talpel, Talwan 112 Talwan

Date of Study:

August 13, 2007 - August 27, 2007

Study Directors:

Kun-Yuan Lin, MOS Pharma Services - Talwan Ltd.

Kuo-Hain Chen, MDS Pharma Services - Tahvan Ltd.

Distribution:

Auslo Pharmaceuticals LLC

This study was conducted according to the procedures described in this report. All data presented are authentic, accurate and correct to the best of our knowledge."

Kun-Yuan Un

Study Director for Artimal Assays

Kun-yuan Lin

Kup-Hata Chen

Koo- Nin Cl

Study Director for Blochemical Assays

flys Chin

Jiaro-Wu Wel, Ph.D Quality Control and Data Reviewer

Jiam - Wei Wei

Peter Chay, Ph.D

Technical Director

PIO 189668 COUR: AURIS

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COOK AUS-13

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SUMMARY

STUDY OBJECTIVE

To evaluate, in Radioligand Binding assays, the activity of compound AUS-132 (PT# 1094968).

METHODS

Mothods employed in this study have been adapted from the scientific literature to maximize reliability and reproducibility. Reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Assays were performed under conditions described in the accompanying "Methods" section of this report. The literature reference(s) for each assay are in the "Literature References" section. If either of these sections were not originally requested with the accompanying report, please contact us at the number below for a printout of either of these report sections.

Where presented, IC_{50} values were determined by a non-linear, least squares regression analysis using Data Analysis Toolbox^{ns} (MDL Information Systems, San Leandro, CA, USA). Where inhibition constants (K_b) are presented, the K_t values were calculated using the equation of Cheng and Prusoff (Cheng, Y., Prusoff, W.H., Blochem, Pharmacol. 22:3099-3108, 1973) using the observed IC_{50} of the tested compound, the concentration of radiologisand employed in the assay, and the historical values for the K₀ of the ligand (obtained experimentally at MDS Pharma Services). Where presented, the Hill coefficient (IC_{50}), defining the slope of the competitive binding curve, was calculated using Data Analysis Toolbox^{ns}. Hill coefficients significantly different than 1.0, may suggest that the binding displacement does not follow the laws of mass action with a single binding site. Where IC_{50} , K_a, and/or IC_{50} data are presented without Standard Error of the Mean (SEM), data are insufficient to be quantitative, and the values presented (K_b, IC_{50} , $IC_$

RESULTS

A summary of results meeting the significance criteria is presented in the following sections. Complete results are presented under the section labeled "Experimental Results". Individual responses, if requested, are presented in the appendix to this report.

SUMMARY/CONCLUSION

Significant results are displayed in the following table(s) in rank order of potency for estimated IC_{50} and/or K_s values.

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Blochemical assay results are presented as the percent inhibition of specific binding or activity throughout the report. All other results are expressed in terms of that assay's quantilation method (see Methods section).

- For primary assays, only the lowest concentration with a significant response judged by the assays' criteria, is shown in this summery.
- Where applicable, either the secondary assay results with the lowest dose/concentration meeting the significance criteria or, if tractive, the highest dose/concentration that did not meet the significance criteria is shown.
- Unless otherwise requested, primary screening in duplicate with quantitative data (e.g., IC50± SEM, IO± SEM and nH) are shown where applicable for individual requested assays. In screening packages, primary screening in duplicate with semi-quantificative data (e.g., estimated ICSO, KI and nH) are shown where applicable (concentration range of 4 log units); available secondary functional assays are carried out (30 µM) and MEC or MIC determined only if active in primary assays >50% at 1 log unit below initial test concentration.
- Please see Experimental Results section for details of all responses.

Significant responses (≥ 50% inhibition or attinulation for Biochemical assays) were noted in the primary assays listed below:

		PRIM	ARY TESTS	,		,	
CAT.#	PRIMARY BIOCHEMICAL ASSAY	8PECIES	CONC. 9	S INH.	IC _{e0} *	Ķ	n _H
220320	Transporter, Departine (DAT)	hum	10 µM	88			
228010	Estrogen ERa	hum	10 pM	93			
228050	Estrogen ERB	hum	10 gM	94			
252010	Transporter, Monoamine	fidden	10 pM				

Pertially soluble in in vitro test solvent.
 A standard error of the mean is presented where results are based on multiple, independent determinations. gp-guines pig; ham-hamater; hum-human

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Col.	TARGET	BATCH	SPP.		CONC.		1% IN	HUBI	TION	IC ₅₀		K	The	1
·.·			•			%	. 100 -50 ↓ ↓	0 :	¥ 100		٠. ·			•
200510	Adenosine A	203049	bum	2	1n -44		<u> </u>	Ť		 				-
200610	Adenosine Aza	203053		2	10 µM	4		١						
200720	Adenosine A	203104	hum	2	Mtq 01	33		1	;					
203100	Adrenensis au	203049	rad tan	2	10 µM	10		12			•			
200200	Adrenergic era	203044	mat	2	10 µM	19		1						
203400	Adrenergic or	203045		2	10 pM	5		Į!					•	
203820	Adrenergic a _M	203048	hum	2	10 µM	8		Ľ.						
203800	Adrenergic or	203048	hum	_	10 pM	5		ľ						
204010	Adrenergic β ₁	203050	hum	2	10 pM	3		L						
204110	Adrenergic β ₂	203051	hune	2	M4 01	15								
204200	Adrenergic B ₂	203051	hum	2	10 µM	20								
204460	Adrenomedulin AM	203460	hune	_	10 µM	-1		1						
204470	Adrenamedulin AM	203481	hum	2	10 µM	-11		4						
204800	Aldosterone	203107	hum	2	10 µM	10		Ľ						
205000	Anaphylatoxin CSa		rat	_	10 µM	11				ł				
295010	•	209237 209102	hum	2 2	10 µM	4		I.						
210020	Androgun (Testosterone) AR Angiotensin AT;	203406	rat	_	10 µM	4	İ	ľ						
210110	·	203095	hum	2	10 µM	2		ľ.						
210700	Anglotensin AT ₂	203482	hum	2	10 µM	4		Ľ						
211000			hum	2	10 pM	21								
211600	Atrial Natriuretic Factor (ANF) Bombesin 881	203189	P	2	10 µM	7		I		1				
211700	Bombesin 882	203483	hure	2	10 pM	3		J)						
211800	Bornbesh 883	203484	hum	5	10 µM	-9		4						
212510	Bradyldnin B.	203485 203088	hum	2	10 µM	-2		١.		1				
212810	Sradykkin B	203087	hum	2	10 pM	5		!		1				
21 381 0	Calcitonin	203087 203238	hum	2	10 pM	3		JI.		İ				
214010			hum	2	10 µM	-4		1						
- 17010	Calcitonin Gene-Related Peptide CGRP ₁	203239	huno	2	10 µM	15				İ				
214510	Calcium Channel L-Type, Benzofriazepine	203056	rat	2	10 µM	27		12						
214800	Calcium Channel L-Type, Dihydropyridina	203057	rat	2	10 рМ	-8		1						
215000	Calcium Channel L-Type, Phenylalkylamine	203058	ret	2	10 µM	28				1				

^{*} Batch: Represents compounds tested concurrently in the same assety(s). ‡ Partially soluble in in vitro test solvent.

estant replacement compounds seaso concurrency in the same assay(s). ‡ Partially counts in who test convent.

† Partially state item meeting criticals for significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity)

| Re-Additional Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Comments | Commen

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Cal.#	TARGET	BATCH	SPP.		CONC.		+% INHIBITION	1Cso	K,	n _H	R
							-100 -55 0 50 100			vyn	
						96	1111		• • •		
216000	Calcium Channel N-Type	203176	rat	2	10 µM	٥					
217020	Cannabinoid CB ₁	203177	hum	2	10 µM	14					
217100	Cannabinoid CB ₃	203178	hum	2	10 µМ	-3					
244600	Chemoticine CX3CR1	203471	hum	2	10 pM	24					
218010	Cholecystokinin CCK, (CCK)	203408	hum	2	10 µM	21					
218120	Chalacystakinin CCK ₂ (CCK ₄)	203458	hum	2	10 µM	-3					
219100	Colchicine	200000	rat	2	10 µM	-15					
219150	Corticotropin Releasing Factor CRF ₁	203409	hum	2	10 µM	-5	I				
219500	Dopamine D ₁	202962	hum	2	10 µM	8	1 2				
219700	Oopamine D ₂₈	202984	hum	2	10 pM	3					
219800	Dopamine D ₃	202985	hum	2	10 µM	3			•		
219900	Dopamine D ₄₃	202968	hum	2	10 µM	7					
220200	Dopamine D _s	202969	hum	2	10 µM	3					
224010	Endothelin ETA	203091	hum	2	10 μМ	-14					
224110	Endothelin ET _B	203082	hum	2	10 µM	14	1				
225510	Epidermal Growth Factor (EGF)	203167	hum	2	10 µM	4	B				
225800	Erythropoletin EPOR	203467	hum	2	10 µM	8	i i				
226010	Estrogen ERa	202976	hum	2	10 µM	93					
228050	Estrogen ERB	202977	mm	2	10 µM	94					
226300	G Protein-Coupled Receptor GPR103	202993	hum	2	10 pM	14	ı				
226230	G Protein-Coupled Receptor GPR8	203470	hum	2	10 µM	0					
225510	GABA, Chloride Channel, TBOB	203101	rat	2	10 µM	-1					
226600	GABA, Flunitrazepam, Central	203081	rat	2	10 µM	. 5	h				
226500	GABA, Muscimol, Central	203080	rat	2	10 pM	-8					
228610	GABA	203158	hum	2	10 µM	-6					
228710	6A8A _m	203159	mun	2	10 pM	2	1				
230000	Gabapentin	203001	rat	2	10 pM	-12					
291510	Galanin GAL1	203165	hum	2	10 µM	-1					
231800	Galanin GALZ	203166	hum	2	10 pM	-6					
232800	Glutamate, AMPA	203157	rat	2	10 µM	1	- 1				

Batch: Represents compounds tested concurrently in the same assay(s), ‡ Partially soluble in in vitro test solvent.
 Denotes lien meeting orients for significance
 † Results with ≥ 50% elimitation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity) R=Additional Comments
 gp=quines ptg; hem-hamster; hum-human

1004968 ADS-132

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Cái.s	· TARGET	BATCH	SPP.	O PP	CONC.		†% in	HIBITIC	N ICso	K,	กผ	B
	•			_		95	·100 ·50	0 X0 1	100			
232700	Glutamate, Kainate	203063	rat	2	10 µМ	24						
232810	Glutamate, NIMDA, Agonism	203064	rat	2	10 µM	29			1			
232910	Glutamate, NMDA, Glycine	203065	rat	2	10 µM	4		1	1			
233000	Glutamate, NM/DA, Phencyclidine	203068	rat	2	10 pM	-6		Ī				
234000	Glutamate, NMDA, Polyamine	203067	ret	2	10 µM	-1	1	d				
239000	Obcline, Strychnine-Sensitive	203088	ret	2	10 µM	-2		7				
239300	Growth Hormone Secretagogue (GHS, Ghrelin)	203243	hum	2	10 µM	0	:					
239910	Histamine H ₃	202970	hum	2	10 µM	5]	1				
239710	Histamine H ₂	203069	hum	2	10 µM	15	1	8	1			
239810	Histamine H	202972	hum	2	10 µM	5	1	ī				
232900	Histamine H _e	202979	hum	2	10 µM	-1	1	ľ				
241000	Imidazoline L. Central	202974	rat	2	10 μ Μ	-6		ì				
242500	Inositol Trisphosphate IPs	203244	rat	2	10 pM	16		1				
243000	Insulin	203208	rat	2	10 μα	-2		, -	1			
250400	Leptin	203317	mouse	2	to µM	12		1 .	1			
250510	Leukotriane, BLT (LTB.)	203353	hum	2	TO µM	-5		1				
250460	Leukotriene, Cysteinyl CystT ₁	203089	hum	2	10 Jan	-18						
250480	Leukotriene, Cysteinyl Cyst 72	203090	hum	2	10 µM	0	'	_				
251100	Melanocortin MC ₁	203411	hum	2	10 µM	7		h				
251300	Melanocortin MC,	203412	hum	2	10 µM .	-1		ſ				
251350	Melanocortin MC,	203413	huro	2	10 µM	6	ŀ	1	1			
251400	Melanocortin MC ₃	203414	hum	2	10 µM	10			1			
251800	Meiatonin NT ₁	203140	hum	2	10 µM	1		1				
251700	Metatonin MT ₂	209142	hum	2	10 µM	33						
252200	Modin	203472	hum	2	Mu Of	14		F	1			
252810	Muscarinic M,	202957	hum	2	10 µM	-2		F	I			
52710	Muscarinic M ₂	202958	hum	2	10 µM	-5		ì	1			
252810	Muscarinic M ₂	202959	hum	2	10 µM	3		"	Ī			
52910	Muscarinic M ₄	202980	hum	2	10 µM	3		i	4			
53010	Muscarinic M ₃	202981	hum	2	10 µM	2		ľ	1			
26100	N-Formyi Peptide Receptor FPRI	203240	hum	2	10 µM	, 3		ď				

^{*} Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partietly soluble in *In vitro* test solvent.

Denotes the misself of children continues in the same assays).
 Partially soluble in in vitro test solvent.
 Partially soluble in in vitro test solvent.
 Results with
 SOM admission or inhibition are highlighted. (Negative values correspond to attraction of binding or enzyme activity)
 Re-Additional Comments
 go-guines pig; ham-hamster; hum-human

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Gat.#	TARGET	BATCH	SPP.		CONC.		†% JNI	HE	ú	TON	IČ ₆₀	K	· n _H	
, . .						96	1	Ĵ.	‡	100		 •		
228200	N-Formyl Peptide Receptor- Like FFRL1	203241	hum	2	الخبر 10	-12						<u> </u>		-
256100	Neuromedin U NMU,	203473	hum	2	المر 10	9		1						
256200	Neuromedin U NMU,	203474	hum	2	10 pM	2		ŀ						
257010	Neuropeptide Y Y ₁	203093	hum	2	Multi	3		ĥ						
257110	Neuropeptide Y Y ₂	203004	hum	2	10 µM	6		ŀ						
258010	Neurotensin NT ₁	203318	hum	2	10 мд	-4		1						
258590	Nicotinic Acetylcholine	202389	hum	2	10 µM	-8		1						
258700	Micothiic Acetylcholine al. Bungarotoxin	202991	hum	2	المامر 10	7		•						
258630	Nicotinic Acetylcholine a7, Bungarotoxin	202990	rat	2	عم ر 10	-7		•						
280110	Opiate & (OP1, DOP)	203070	hum	2	10 µM	اه		ł						
280210	Oplate x (OP2, KOP)	203072	hum	2	10 µM	11		8						
280410	Oplate µ (OP3, MOP)	203074	hum	2	10 µM	-4		ď						
280800	Orphanin ORL	203478	hum	2	10 pM	4	7	١,						
284500	Phorbol Ester	203076	mouse	2	10 µM	8	9	ľ						
265010	Platelet Activating Factor (PAF)	203007	hum	2	10 pM	12		-						
286200	Piztelet-Derived Growth Factor (PDGF)	202979	mouse	2	16 pM	9		Ī						
265500	Potassium Channel [K,]	203079	rat	2	10 µM	٥				ı				
265600	Potassium Charmel [Kerr]	203078	ham	2	10 μм	-12	1	ı						
265600	Potassium Channel [SKo]	203002	rat	2	10 µM	3	•	1						
65900	Potassium Channel HERG	202994	hum	2	10 µM	-18	1	ď						
68020	Progesterona PR-B	202992	hum	2	10 µM	17								
65030	Prostanoid CRTH2	203352	hum	2	10 pM	-8	1	1						
68050	Prostanoid DP	202986	hum	2	10 µM	21	•		1					
268200	Prostancid EP;	202998	hum	2	10 µM	18				ı				
68410	Prostanoid EP.	202997	hum	2	10 µM	0		٢		ı				
86510	Prostanoid, Thromboxane A ₂ (TP)	203271	hum	2	10 µM	-15								
68700	Purtnergic Pa	202982	rabbit	2	10 µM	15								
68810	Purinergic Pay	202983		2	10 µM	7		5		- [
69500	Retinoid X Receptor IXXIa	203477		2	10 µM	3		ļ.		- 1				

^{*} Batch: Represents compounds tested concurrently in the same assay(e), ‡ Partially soluble in in vitro test solvent.

escale represents compounds testant concurrency in the same assay(e). ‡ Perceily soluble in in vitro test solvent.

† Results with ≥ 50% attraction or inhibition are highlighted. (Negative values correspond to attraction of binding or enzyme estivity) R—Additional Commonts

gp—guines pig; ham—hamater; hum—human

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Cet.#	TARGET	BATCH	SPP.		CONC.	1	†% IN	HBI3	TON	-IC _{so}	. :	K	. m	R
					,	- %	↓ ↓ ↓ ↓	ů	1 100		٠.			٠,
270000	Rollpram	203130	rat	2	Nu Of	2		1	·					
270300	Ryanodine RyR3	203478	rat	2	10 pM			ľ						
271110	Serotonin (5- Hydroxytryptemine) 5-HT1A	203108	hum	2	10 µМ	-8		1						
271200	Serotonin (S- Hydroxytryptamine) S-HT ₁₈	203109	ræt	2	10 µM	19								
271700	Serotonin (5- Hydroxytryptamine) 5-HT ₂₉	203251	hum	2	10 pM	10		•						
271800	Serotenin (5- Hydroxytryptamine) 5-HT _M	203273	hum	2	10 µM	13		•						
271910	Serotonin (5- Hydroxytryptamine) S-HT ₃	203184	hum	2	10 µM	-5		1						
272000	Serotonin (5- Hydroxytryptamine) 5-HT _e	203174	EP	2	10 µM	10		1						
272100	Serotonin (S- Hydroxytryptamine) S-HT _M	203003	hum	2	10 µM	4								
272200	Serotonin (5- Hydroxytryptamine) 5-HT ₆	203254	hum	5	10 µM	26								
278110	Sigma o ₁	203082	hun	2	10 µM	7		h						
278200	Sigma o ₂	203083	ret	2	10 µM	14								
279510	Sodium Channel, Site 2	203084	rat	2	10 µM	11								
282510	Somatostatin sst1	203181	hum	2	10 µM	6		li l						
282700	Somatostatin sst2	203182	hum	2	10 µM	3		li						
282530	Somatostatin sst3	203183	hum	2	10 рм	15								
282900	Somatostatin sst4	203184	hura	2	Mu 10	-1		ľ						
283000	Somatostatin sstS	203185	hore	2	10 µM	-13	· 1							
255510	Tachytinin NK;	203160	hors	2	10 µM	2		-						
55600	Tachytinin NK	203161	hum	2	10 µM	17								
55710	Tachytinin NK ₃	203162	hum	2	10 µM	1		1						
95800	Thyroid Hormone	203171	rat	2	10 µM	14								
288000	Thyrotropin Releasing Hormone (TRIO	203259	rat	2	10 µM	-15	1		*					
88200	Transforming Growth Factor- β (TGF- β)	202980	mouse	2	10 JdM	10		1						
02000	Transporter, Adenosine	203088	gp	2	10 µM	7		1						
19000	Transporter, Choline	203105	rat	2	10 µM	17		I _	- 1					•

^{*} Baich: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in in vitro test solvent.

Pendia has conting orients to significance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Nagative values correspond to <u>stimulation</u> of binding or enzyme activity)

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† Results with ≥ 50% stimulation or inhibition are highlighted.

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cut.	TARGET	BATCH	SPP.	(C)	CONC.	. 1	% inhibition	iC ₅₀ K ₁ n _H R
<u> </u>	· <u>· </u>					96	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
4 220320	Transporter, Dopamine (DAT)	203188	hum	2	10 µM	88		
226400	Transporter, GABA	203059	rat	2	10 pM	8		
\$ \$2010	Transporter, Monoamine	203425	rabbit	2	10 pM	51		· •
204410	Transporter, Norepinephrine (NET)	203054	hum	2	10 µM	37		
274030	Transporter, Serotonin (5- Hydrmytryptamine) (SERT)	203055	hum	2	10 µM	17	3	
286700	Urotensin II	203234	חוטל	2	10 µM	-15		
288810	Varilloid	203133	rat	2	10 µM	-9		
286900	Vascular Endothelial Growth Factor (VEGF)	203041	hum	2	10 µM	6	1	
267010	Vasoactive Intestinal Peptide VIP ₁	203260	hum	8	10 µM	-9	ŧ	
287620	Vasopressin V _M	203097	hure	2	10 µM	2	1	
287560	Vasopressin V ₁₈	203088	huro	2	10 µM	-11		
287610	Vasopressin V ₃	203099	hura	2	10 pM	-18		
288000	Vitamin D ₂	203098	hum	2	10 pM	-1		

gp-guinea pig; ham-hamster; hum-human

^{*} Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in in vitro test solvent.

• Denotes here receding orienta for eignificance

† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)

R=Additional Commonits

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

. . .

MDS has an exclusive, worthride limited use license from Synaptic Pharmaceutical Corporation to perform these assays: Advanergic Alpha 1D, Advanergic Alpha 2B, and Doparnine D5 for salety and selectivity profiling. MDS' license excludes performing those assays in consection with drug discovery or development activities where the principal therepeutic machanism of action of the test compound involves selective binding to a licensed receptor. Customers may contact Synaptic directly if they believe they need a broader license.

SpectrumScreen Data Report Ausio Pharmaceuticals LLC

Study Completed: August 27, 2007 Report Printed: August 27, 2007

MDSPS PT#: 1094969

Alt. Code 1: Batch: NW037/07

Alt. Code 2:

Alt. Code 3:

Sample(s): AUS-133

M.W.: 242.27

Objectives:

To evaluate, in SpectrumScreen, the activity of test compound AUS-133 (PT# 1094969).



1094969

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MDS Pharma Services Pharmacology Data Report On Compound AUS-133 For Ausio Pharmaceuticals LLC

Work Order Number:

1-1028408-1

Services Being Reported: SpectrumScreen

Alternative Work Order No:

Purchase Order Number:

Total # of Assays: 159

Compound information:

Compound Code:

AUS-133

Alternative Code 1:

Batch: NW037/07

Alternative Code 2:

Alternative Code S:

MDSPS Internal #:

1094989

Molecular Weight:

242.27

Sponsor:

Ausio Phermaceuticets LLC

1776 Mentor Averue Suite 340

Cincinned, OH 45212 USA

Undertaken at:

MDS Pharma Services - Talwan Ltd.

Pharmacology Laboratories 158 Li-Teh Road, Peltou

Tatpal, Tatwan 112 Tatwan

Date of Study:

August 13, 2007 - August 27, 2007

Study Directors:

Kun-Yuan Lin. MDS Pharma Services - Tahvan Ltd.

Distribution:

Kuo-Hain Chen, MDS Pharma Services - Talwan Ltd. Auslo Pharmaceuticals LLC

"This study was conducted according to the procedures described in this report. All data presented are authentic, accurate and correct to the best of our knowledge."

Kun-Yuan Un

Study Director for Animal Assays

Kem- Juan Lin

Kuo-Hain Chan

Study Director for Biochemical Assays

25. Ain

Earn-Wu Wel, Ph.D Quelty Control and Date Reviewer

Jiam - Wee Wer

Peter Chiu, Ph.D

TTE IDOOS CODE ADS 11

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COME AUS 133

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SUMMARY

STUDY OBJECTIVE

To evaluate, in Radioligand Binding assays, the activity of compound AUS-133 (PT# 1094969).

METHODS

Methods employed in this study have been adapted from the scientific literature to maximize reliability and reproducibility. Reference standards were run as an integral part of each assay to ensure the validity of the results obtained. Assays were performed under conditions described in the accompanying "Methods" section of this report. The literature reference(s) for each assay are in the "Literature References" section. If either of these sections were not originally requested with the accompanying report, please contact us at the number below for a printout of either of these report sections.

Where presented, IC₅₀ values were determined by a non-linear, least squares regression analysis using Data Analysis Toolbox^{7M} (MDL Information Systems, San Leandro, CA, USA). Where inhibition constants (K_b) are presented, the K_t values were calculated using the equation of Cheng and Prusoff (Cheng, Y_n Prusoff, W.H., Blochem. Pharmacol. 22:3099-3108, 1973) using the observed IC₅₀ of the tested compound, the concentration of radiologand employed in the assay, and the historical values for the K_b of the ligand (obtained experimentally at MDS Pharma Sarvices). Where presented, the Hill coefficient (I_b), defining the slope of the competitive binding curve, was calculated using Data Analysis Toolbox^{7M}. Hill coefficients algalificantly different than 1.0, may angest that the binding displacement does not follow the laws of mass action with a single binding site. Where IC₅₀, K_b, and/or n_H data are presented without Standard Error of the Mean (SEM), data are insufficient to be quantitative, and the values presented (K_b, IC₅₀, n_h) should be interpreted with caution.

FEBULTS

A summary of results meeting the significance criteria is presented in the following sections. Complete results are presented under the section labeled "Experimental Results". Individual responses, if requested, are presented in the appendix to this report.

SUMMARY/CONCLUSION

Significant results are displayed in the following table(s) in rank order of potency for estimated IC₅₀ and/or K₄ values.

SUMMARY OF SIGNIFICANT PRIMARY RESULTS

Blochemical assay results are presented as the percent inhibition of specific blocking or activity throughout the report. All other results are expressed in terms of that assay's quantitation method (see Methods section).

- For primary assays, only the lowest concentration with a significant response judged by the assays' oritoria, is shown in this summary.
- Where applicable, either the secondary assay results with the lowest dose/concentration meeting the significance criteria or, if inactive, the highest dose/concentration that did not meet the significance oriteria is shown.
- Unless otherwise requested, primary screening in duplicate with quantitative data (e.g., ICSO± SEM, KI± SEM and nH) are shown where applicable for individual requested assays. In screening packages, primary screening in duplicate with semi-quantitative data (e.g., estimated ICSD, KI and nH) are shown where applicable (concentration range of 4 log units); available secondary functional assays are carried out (SO µM) and MEC or MIC determined only if active in primary assays >50% at 1 log unit below initial test concentration.
- Please see Experimental Results section for details of all responses.

Significant responses (≥ 50% inhibition or attrautation for Elochemical assays) were noted in the primary assays listed below:

	4.	PRIM	ARY TESTS			
CAT.	Primary Biochemical assay	SPECIES	CONC. % IN	IB. K.	. К	Гы
204410	Transporter, Norepinephrine (NET)	hum	10 рм 50		•	
220320	Transporter, Dopamine (DAT)	hum	10 µM 92			
226010	Estragen ERa	hum	10 µM 94			
228050	Estrogen ERB	hum	88 Mu 01			

Partially solubio in in vitro test solvent.
 A standard error of the mean is presented where results are based on multiple, independent determinations.
 go-guines pig; ham-hamster; hum-human

PTW 1094969 COOE AUS-113

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Cer.A	TARGET	BATCH*	SPP.		CONC.		†% I	(HIBI)	TON	IC.	к	• •	•	- 1
77.7	•	٠.											e i M	
	 	· ·.				96	11				V.;	٠,		
200510	Adenosine A ₄	203049	hum	2	10 µM	 	ł							
200610	Adenosine Aga	203053 -	hum	2	10 pM	24				1				
200720	Adenosine As	208104	מעל	2	10 µM	15				1				
203100	Adrenergic or _{th}	203043	rat	2	10 µM	9								
203200	Adrenergic a ₁₀	203044	rat	2	10 µM	2		l l		İ				
203400	Adrenergic are	203045	hum	2	10 µM	- 8	İ	ı İ						
203820	Adrenergic as	203048	hum	2	10 µM	10		1						
203800	Adrenergic a _K	208048	hum	2	10 July	5		Į,						
204010	Adrenergic \$1	203050	hum	2	10 µM			i						
204110	Adrenergic \$2	209051	hum	2	10 µM	6		li						
204200	Adrenergic β ₃	203052	hum	2	10 µM	-5	1							
204460	Adrenomeduttin AM	203460	hum	2	10 µM	-2		i						
204470	Adrenomedullin AM	203461	hun	2	10 µM	9		1						
204800	Aldosterone	209107	rat	2	Mų Of	20								
205000	Anaphylatoxin C5a	203237	hum	2	10 µM	.7								
285010	Androgen (Testasterone) AR	203102	rat	2	10 pM	5		1						
10020	Angiotensin AT,	208408	hum	2	10 µM	-14								
210110	Angiotensin AT ₂	203095	hum	2	10 pM	1		-[h						
210700	API	203482	hum	2	10 µM	-10		1						
11000	Atrial Natriuretic Factor (ANF)	203189	æ	2	10 µM	4		1						
11800	Bombesin B81	203483	hum	2	10 µM	7		li						
11700	Bombesin 882	203484	hum	2	10 µM	-1		ľ						
11800	Bombesin BB3	203485	hum	2	10 µM	-12								
12510	Bredykinia B ₁	203086	hum	2	10 µM	8		1						
12810	Bradylinia 8,	203087	hum	2	10 µM	13								
18810	Calcitonia	203238	hum	2	10 рм	-1			-					
	Calcitonin Gene-Related Pepuide CGRP ₁	203239	hum	2	10 pM	8		þ						
	Calcium Channel L-Type, Benzothiazepine	203056	rat	2	10 pM	21								
	Calcium Channel 1-Type, Ditrydropyridine	203067	rat	2	10 µM	0								
	Calcium Channel L-Type, Phonylalkylamina	203068	nt	2	10 pM	38								

^{*} Batch: Represents compounds tested concurrently in the same assay(s), ‡ Partially soluble in in vitro test solvent,

4 Denotes it is a mooting criteria for eignificance

† Results wit: ₹ 50% stimulation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)

R=Additional Comments

gp=guines pi_; htm=hamster; hum=human

PIN. 1094969 AUS-113

Cet.#	TARGET	BATCH*	SPP.	D=	CONC.		†% IN	HUBITION	I IC _{so}	Ř			R:
	•	·.	٠					0 20 10 0 20 10	1		•••	That	10
· · · ·		•				95	1 1	+ 1 1	<u> </u>		•	:	
21 5000	Calcium Channel N-Type	203178	rat	2	10 pM	I⊸	ĺ	1					
217020	Cannabinoid CB ₁	203177	hum	2	10 µM	11		1					
217100	Cannabinoid CB ₂	203178	hum	2	10 µM	6		1					
244600	Chemokine C/G/CR1	203471	hum	2	Mپ 10	11		1					
218010	Chalecystokinin CCK, (CCK)	203408	hum	2	40ب 10	20			ļ				
218120	Cholecystokinin CCIG (CCIG)	203468	hum	2	10 µM	,	4	F	1				
219100	Colchicine	203000	rat	2	10 uM	22							
219150	Corticotropin Releasing Factor CRFs	203409	hum	2	10 µM	-3	•	r					
219500	Copamine D	202962	hum	2	10 pM	٥	ŀ]				
219700	Dopamine D ₂₅	202884	hum	2	10 µM	-5		il	1				
219800	Dopamine D ₃	202985	hum	2	10 pM	-5		il.					
219900	Dopamine Du	202988	hum	2	10 pM	11		1					
220200	Dopamine D ₃	202969	hum	2	10 pAJ	7		1					
224010	Endothelin FTA	203091	hum	2	10 µM	-5	1	ď	l				
224110	Endothelin ETa	203082	hum	2	10 µM	2	l .	ች	l				
225510	Epidermal Growth Factor (EGF)	203187	hum	2	10 µM	-6		1					
225800	Erythropoletin EPOR	203889	hum	2	10 µM	3	l .	1,	1				
228010	Estrogen ERa	202976	hum	2	10 µM	94	ŀ		1				
228050	Estrogen ERB	202977	hum	2	10 Mu	98							
226300	G Protein-Coupled Receptor GPR103	202993	hum	2	10 pM	38							
226230	G Protein-Coupled Receptor GPR8	203470	hum	2	10 µM	1		1					
226610	GABAL Chloride Channel, TBOB	203 to 1	rat	2	10 µM	3		1					
226600	GABA, Flunitraceparn, Central	203061	rat	2	10 µM	1		h	ŀ				
228500	GABA, Muscimol, Central	203080	rat	2	10 µM	-1		ď	ł				
228810	GABASIA	203158	ham	2	10 µM	-1		1					
228710	GABA ₆₁₈	203159	hum	2	10 pM	-6		1	l				
230000	Gebapenun	203001	rat	2	10 pM	-17	ı						
231510	Galanin GAL1	203165	hum	2	10 µM	-5		7					
231600	Galanin GAL2	203166	hum	2	10 µM	-3		7					
232800	Clutemate, AMPA	203157	rat	2	10 µM	-6		3					

^{*} Batch: Represents compounds tested concurrently in the same assay(s), ‡ Partially soluble in in vitre test solvent.

4 Denotes item meeting criteria for significances

† Results with \$ 50% attrudation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)

ReAdditional Comments

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-Cat.#	TARGET	BATCE	SPR	15 00	CONC.		†% JNI	31811	TON	IC ₅₀	16	n _e R
<u> </u>		• .				95	400 00 ↓ ↓	1 1				
232700	Glutamate, Kalnate	203063	ret	2	70 µM	18						
232810	Glutamate, NMDA, Agonism	203064	ret	2	10 µM	24						
232910	Glutamate, NMDA. Glycine	203065	rat	2	10 μω	-5	i					
233000	Glutamate, NMDA, Phencyclidine	203066	rat	2	10 pM	9					•	
234000	Glutamate, NMDA, Polyamine	203007	rat	2	10 µM	6		ŀ		}		
239000	Glycine, Strychmine-Sensitive	203068	rat	2	10 μм	12	1	9				
239300	Growth Hormone Secretzgogue (GHS, Ghrelia)	203243	pran	2	10 μм	12				ĺ		
239610	Histornine H,	202970	hum	2	10 µM	11				l		
239710	Histamine H ₂	203069	hum	2	10 pM	7		1	1]		
239810	Histamine H ₃	202972	hum	2	10 µM	18				l		
239900	Histonine Ha	202973	ព្រាលា	2	10 µM	-1						
241000	Imidazoline I _I , Central	202974	rat	2	10 µM	-13	1	J				
242500	Inositol Trisphosphate IP3	203244	rat	2	10 pM	11		-				
243000	Insutin	203208	rat	2	10 µM	-2		1				
250400	teptin	203317	mouse	2	10 pM	2		7				
250510	Leukotriene, BLT (LTB.)	203353	hum	2	10 µM	-25		•				
250480	Leukotriene, Cystelnyl CysLT,	203089	hum	2	10 µM	3		1				
250480	Leukotriene, Cystelnyl Cyst.T ₂	203090	hum	2	10 µM	-49	.)··	ľ				
251100	Melanocortin MC ₁	203411	hum	2	10 µM	1],				
251300	Melanocortin MC ₃	203412	hum	2	10 рМ	-6		ľ				
251350	Melanocortin MC4	203413	hum	2	10 μM	3	'	lı 💮				
251400	Melanocortin MCs	203414	hum	2	10 pM	8		i				
251600	Melatonin MT ₁	203140	hum	2	10 рм	14						
251700	Melatonia MT ₂	203142	hum	2	10 µM	48						
252200	Motilin	203472	tum	2	10 pM	-1						
252610	Muscarinic M ₁	202957	hum	2	TO pM	3		1				
252710	Muscarinic My	202958	hum	2	10 pt.4	4		ľ	ļ			
252810	Muscarinic Ma	202959	hum	2	10 pM	0		Ì	ı			
252910	Museurinic M _e	202960	hum	2	10 pM	8		ı				
258010	Muscarinic Ms	202981	tum	2	10 pM	-1	1	1				
228100	N-Formyl Peptide Receptor [PR]	203240	hum	2	10 pM	-6	i		-			

Balch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in in vitro test solvent.

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† Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to alimitation of binding or enzyme activity) R=Additional Comments

gp=guines pig; harm-harmster; hum-human

CODE.

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cat.#	TARGET	BATCH	SPP.	the	CONC.		% INBI	BITTON	IC ₅₀	K	Пн	Ŕ
				•			100 -50 8	30 too	100		''18	~ .
	· · · · · · · · · · · · · · · · · · ·					96	1 + †	1 1			``	
228200	N-Formyl Peptide Receptor- Like FPRL1	203241	hum	2	10 µM	-7	1					
256100	Neuromedin U NMU,	203473	hum	2	10 µM	8		1				
256200	Neuromedin U NMU,	203474	hum	2	10 µM	-5	1	•				
257010	Neuropeptide Y V _i	203099	hum	2	10 µM	7						
257110	Neuropeptide Y Y ₂	208084	hum	2	10 pM	6	ŀ					
258010	Neurotensin HT ₁	203318	hum	2	10 µM	اه ا	2	•				
258590	Nicotinic Acetylcholine	202989	hum	2	10 µM	-6	1					
258700	Nicotinic Acetylcholine at , Bungarotaan	202991	hum	2	10 pM	12						
258830	Mcotinic Acetylcholine of. Bungarotoxin	202990	rat	2	10 µM	2		1				
260110	Oplate & (OP1, DOP)	203070	hum	2	10 µM	12						
260210	Opiate x (OP2, KOP)	203072	hum	2	10 µM	16	i	8				
280410	Optate µ (OP3, MOP)	203074	hum	2	Mu Of	-9	al'					
260600	Orphanin ORL ₁	203476	hum	2	10 pM	7	1,					
264500	Phorbol Ester	203078	mouse	2	10 pM	.9		'i				
265010	Platelet Activating Factor (PAF)	203007	hum	2	10 post	9	-1	. [
265200	Platelet-Derived Growth Factor (PDGF)	202979	mouse	2	10 µM	9						
265500	Potassium Channel [Ka]	203079	rat	2	10 µM	-1	d					
265600	Potassium Channel Kcal	206078	ham	2	10 µM	-8	- 1	I				
265800	Potassium Channel (SKo.)	203002	ret	2	10 µM	2	1	l				
265900	Potassium Channel HERG	202994	hum	2	10 µM	8	i.	. 1				
68020	Progesterone PR-B	202992	hum	2	10 µM	15		2				
268030	Prostanoid CRTHZ	203352	hum	2	10 µМ	9	li li	•				
288050	Prostanoid DP	202995	hum	2	10 µM	29	ľ					
68200	Prostanoid EP ₂	202996		2	10 µM	14						
68410	Prostanoid EP.	202997	hum	2	10 pM	7	ľ					
85 510	Prostanoid, Thromboxane A ₂ (IP)	203004		2	10 pM	-7	4				•	
88700	Purinergic Pas	203308	rabbit	2	10 yMs	8	l,					
268810	Purinergic P _W	202983	rat	2	t0 pM	3	ľ					
69500	Ratinoid X Receptor RXRa	203477		2	10 pM	2	l'	- 1				

^{*} Batch: Represents compounds tested concurrently in the same accepts). ‡ Partially soluble in in vitro test solvent.

go-guirus pig; ham-hamater; hum-human

Denotes then masting criteria for algorithments in the same assertion. Partially soluble in in vitro test solvent.
 Results with 2 60% climatation or inhibition are highlighted. (Negative values correspond to stimulation of binding or enzyme activity) R=Adultional Comments.

EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

Cot.#	TARGET	BATCH•	SEP	10=	CONC.	†% INHIBITION			IC ₅₀	Κ. (nu R
				•	•		1 1 1				
270000	Rolipram	203130	rat	2	Mu Of	13	i			<u> </u>	
270300	Ryanodine RyR3	203478	rat	2	Mu OI	4					
271110	Serotonin (5- Llydroxytryptamine) 5-HT _{In}	203108	hum	2	10 µM	2					
271 200	Serotonia (5- Hydrwytryptarrine) 5-HT ₁₃	203109	ret	2	10 µM	19					•
271700	Scrotonia (5- Hydrwytryptamina) 5-HT ₂₈	203251	tum	2	10 µM	25	þ				
271800	Serotodin (5- Hydroxytyptamine) 5-HT ₂₆	203273	hum	2	10 µM	9	ļ	1			
271910	Scrotosin (5- Hydrosytryptamine) 5-HT ₃	203184	hum	2	10 µM	0	}				
272000	Serotonin (3- I lydrogstyptamine) 5-HT4	203174	gp	2	10 pM	8					
272100	Serotonin (3- Hydroxytyptamine) 5-HTF _{SA}	203003	hum	2	10 µM	3	þ				
272200	Scrotorin (5 Hydrootryptamine) 5-HT ₄	203254	hum	2	10 µM	27					
278110	Sigma o ₁	203082	hum	2	المير 10	1	h				
278200	Sigma o ₂	203083	ret	2	10 µM	18	i	. !			
276510	Sodium Channel, Site 2	203084	rat	2	10 µM	12		i 1			
282510	Somatostatin asti	203181	hwn	2	10 µM	8	li	i			
282713	Somatostatin sst2	203182	hum	2	10 pM	-11	1	· [
282530	Sometustatin sst3	203183	hum	2	10 μ44	8	1				
282900	Somatostatin sst4	203184	hum	2	10 µth	12	İ				
283000	Somatostatin sst5	209185	hum	2	10 µM	-11	8	1			
255510	Tachyklidin NK,	203160	hura	2	10 paM	10	- 1				
255600	Tachykinin NK,	203161	hum	2	10 µM	22	i i				
255710	Tachykinin NK,	203182	hum	2	10 µM	0	ľ	-			
285010	Thyrold Hormone	203171	rat	2	10 pM	0	1	j			
2887"3	Thyrotropin Releasing Hormone (TRH)	203259	ret	2	10 рм	1	þ				
288209	Transforming Growth Factor-B (TGF-B)	202980	mouse	2	10 µM	8	þ				
202000	Transporter, Adenosine	203088-	gp.	2	10 pM	6	h	1			
219000	Transporter, Choline	203105	rat	2	10 µM	-13					

gp-grinca pig; ham-hamster, hum-human

^{*} Batch: Represents compounds tested concurrently in the same assay(s). ‡ Partially soluble in in vitro test solvent.

• Do: Les kern mesting criteria for significance

† Ro · 1s with ≥ 50% etimulation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity)

R=Ac. Sand Comments

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Cat. #	TARGET	BATCH	SPP.	(D)	CONC.	1% INHUBITION ICso K nin					
N.						96	1 1 1 1 1 0 00 00	100		Kr rig R	
* 5503JJ	Transporter, Doparnine (DAT)	203188	hum.	2	10 pM	82			-		
226400	Transporter, GABA	203297	rat	2	10 AA	12			•	14. C. S.	
252010	Transporter, Monoamine	203179	rabbit	2	10 µM	48		- 1			
204410	Transporter, Norepinephrine (NET)	· 203054 ·	hum	2	10 µM ;	50		1		en Sportson Agreement Tagens	
274030	Yransporter, Serotonin (5- Hydronytryptamine) (SERT)	203055	hum	2	May Of	15	13		•	* *	
288700	Urotensin B	203234	hum	2	10 µM	-16		- 1			
288810	Vanilloid	203133	rat	2	10 pM	-3	7				
2869^1	Vascular Endothelial Growth Factor (VEGF)	208041	hum	2	10 µM	-3					
2870 15	Vasoactive tritestinal Peptide VIP	203260	hum	2	10 µM	-1	1				
28757)	Vasopressin V _{IA}	203097	hum	2	10 µM	-1	ı	1			
287560	Vasopressin V ₁₃	203098	hum	2	10 µM	-14	8	- 1			
2876:0	Vasopressin V,	203099	hum	2	10 µM	-19		1			
288000	Vilamin D,	203098	hum	2	10 µM	-9					

^{*} Batch: Represents compounds tested concurrently in the same essay(s). ‡ Partially soluble in in vitro test solvent.

• Donotes item meeting orients for algorificance

[†] Results with ≥ 50% stimulation or inhibition are highlighted. (Negative values correspond to <u>stimulation</u> of binding or enzyme activity) pp—graines pig; ham-hamster; hum-human

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EXPERIMENTAL RESULTS - BIOCHEMICAL ASSAYS

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